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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/644,289	05/10/96	KULESZ-MARTIN M	RPP:135D-US

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EXAMINER	
EYLER, Y	
ART UNIT	**PAPER NUMBER**
1642	19

DATE MAILED: 02/01/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/644,289	Applicant(s) Kulesz-Martin
	Examiner Yvonne Eyler	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Nov 10, 1999*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 3-6, and 8-19* is/are pending in the application.

Of the above, claim(s) *12-14* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3-6, 8-11, and 15-19* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1, 3-6, and 8-18 are pending in the application. Claims 12-14 have been withdrawn from further consideration. Claims 1, 3-6, 8-11, and 15-18 are under consideration.

Claim Rejections Maintained:

3. The rejection of Claims 1, 3-6, 8-11 , 15, 17 and 18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Applicant argues that one of even meager skill in the art would understand the metes and bounds of the claimed invention and makes reference to the 58 citations in the information disclosure statement. Applicant further argues that Harris et al. is improperly cited since it is post-filing date information.

These arguments have been considered but are not found to be persuasive. Initially, it is noted that post-filing date art, while not able to serve as a 102 or 103 reference, may be applied in support of rejections under U.S.C. 112 first and second paragraphs. Harris et al. teaches that the "activity" of p53 is dependent on conditions and thus the term "active" absent further information was unclear even about six months after filing of the instant application. The citation of 58 references as evidence, many of which do not address p53 "functions" or "growth regulatory

activity" is not found to clarify the indefinite terms. It is suggested that one way that applicant could overcome the indefiniteness is by removing the vague and indefinite terms from the claim language and claiming the p53as molecule to only differ from wildtype p53 within the final 50 carboxy terminal amino acids by lacking a negative regulatory domain and by comprising a sequence encoding SEQ ID NO: 1, for example.

4. The rejection of Claims 16 and 19 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Applicant argues that the determination of subsequences which raise and antibody response is art-standard. This is not found to be persuasive because there is no definition of what constitutes a portion such that one of skill could obtain and test it. Is a portion linear? Is a portion contiguous? How big is a portion?

5. The rejection of Claims 1, 3- 6, 8-11, 17, and 18 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

Applicant argues that since the only difference between p53 and p53as is in the C-terminus, that it is clear that the antibodies which selectively bind p53as over p53 are raised to the unique terminal portions. This is not found to be persuasive because no actual epitopes are disclosed by the specification. An epitope may be linear or conformational, which in the latter

situation would involve sequences other than the terminal portions. The disclosure of a selective antibody does not provide sufficient description of an epitope. Further, the specification does not contemplate the addition of exogenous, non-p53, sequences, such as his-tag epitopes.

6. The rejection of Claims 1, 3-6, 8-11, 17, and 18 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

Applicant argues that one of skill in the art would know how to modify the C-terminus and to add an unique epitope. Applicant argues that the invention is directed to the concept of eliminating the negative regulatory domain and incorporating an unique epitope, which concepts may be practiced by one of minimal skill. This is not found to be persuasive because the specification did not identify the epitope within the C-terminal region to which unique antibodies bind. As made of record, identification of an epitope, versus a peptide which raises an antibody response or is bound by an antibody, is complex and often includes non-linear sequences. Thus, the specification, while providing objective evidence that antibodies which are selective for p53as may be raised, the epitope to which they bind it not provided, nor is sufficient guidance provided in the identification of the epitope to which those antibodies bind provided. Further, the specification teaches specific manipulations which eliminate the negative regulatory domain and apparently maintain all other p53 functions (the indefiniteness of which is discussed supra and of record). While the concept of truncating, substituting, etc. such that a specific domain is

eliminated may be enabled, the maintenance of unknown functions while doing so is not for the reasons discussed supra and of record in the previous office actions. Thus, the concept of the **specific** manipulations applied to the C terminus is sufficiently taught by the specification, however, the manipulation to create an epitope or to maintain unknown functions, as claimed is not sufficiently enabled by the specification as filed.

7. The rejection of Claims 16 and 19 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasmids or viral vectors containing SEQ ID NO:1, does not reasonably provide enablement for plasmids or viral vectors containing any portion of SEQ ID NO:1 is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant argues that one of minimal skill would be enabled to easily determine whether a portion raises an antibody. These argument is not found persuasive for reasons of record supra with regard to the rejection of claims 16 and 19 under 112 U.S.C. second paragraph and for reasons of record in the previous office action. Given the indefiniteness of the metes and bounds, the number of substituted, deleted "portions" that are encompassed, which "raise an antibody response" which is not limited to a specific response, one of skill would be enabled to identify if they were in possession of a portion or not.

8. The rejection of Claims 1, 3-5, 8-11, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolf et al (IDS; Mol. Cell Biol. 5:127-132, 1985) or Arai et al.(IDS; Mol. Cell Biol. 6:3232-3239, 1986) is maintained for reasons of record.

9. The rejection of Claim 6 under 35 U.S.C. 103(a) as being unpatentable over Wolf et al (Mol. Cell Biol. 5:127-132, 1985) or Arai et al. or Arai et al (Mol. Cell Biol. 6:3232-3239, 1986) as set forth above regarding claims 1, 3-5, 8-11, 17 and 18 in view of Lee et al (IDS; EP 529160) is maintained for reasons of record.

Applicant argues that prior responses have pointed out significant differences between this cited art and the claimed invention.

Applicant argues that M-8 and p53as are not the same due to internal mutations other than the C-terminal differences. This argument is not found to be persuasive for reasons of record. Namely, the claims do not specify that the p53 to which p53as is compared be wildtype p53. If one refers the p53as of Wolf et al. or Arai et al. to the mutant p53 molecules from which they are derived, they meet the claim limitations. Amendment to recite sequential identity up to the final 50 carboxy terminal amino acids of **wildtype** p53 would overcome the basis of the rejection.

10. The rejection of Claims 1, 3, 4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (Nuc.Acids Res. 20:1979-1981, 1992), in view of Sambrook et al. Molecular Cloning, A laboratory Manual. Second Ed. Cold Spring Harbor Laboratory Press. 1989) is maintained.

Applicant continues to argue that the rejection is based on impermissible hindsight and that it would not be obvious to clone full-length p53as from the teachings of Han et al. in combination with those of Sambrook et al. because Han et al. teach only the sequencing of segments of p53as and never incorporate whole p53as into a plasmid. Applicant maintains that Sambrook et al. does not remedy the failings of Han et al.

These arguments are not found to be persuasive for reasons of record. While Han et al. do not clone full-length p53as, they teach the art known presence of full length p53as and that it's study was critical to future studies of p53. Han et al. further provide primers unique to p53as and identify the unique regions. Han et al. do not clone full length p53as, however, it is not required of a 103 reference to completely disclose the invention and the failure to do so does not render the obviousness of the invention based on that reference based on hindsight. Given the knowledge of p53as and it's criticality in the studies of p53, plus the primers necessary to isolate the p53as cDNA, plus the art-known procedures for doing so supplied by the textbook of Sambrook et al., it would have been *prima facie* obvious to one of ordinary skill in the art to further the cloning of Han et al. to include full-length p53as, with a reasonable expectation of success given the provision of primers for doing so and the art-standard techniques of Sambrook et al. Further, one would be motivated to do so given the suggestion by Han et al. that it would be critical to include p53as in the study of p53.

11. The rejection of Claims 5, 6, 8-11, and 18 under 35 U.S.C. 103(a) as being unpatentable over Han et al (Nuc.Acids Res. 20:1979-1981, 1992), in view of Lee et al (IDS; EP 529160) is maintained for reasons of record.

Applicant argues as above, that the rejection is based on impermissible hindsight and that it would not be obvious to clone full-length p53as from the teachings of Han et al. in combination with those of Lee et al. because Han et al. do not teach incorporation of whole p53as into anything. Applicant maintains that Lee et al. does not remedy the failings of Han et al.

These arguments are not found to be persuasive for reasons of record. While Han et al. do not clone full-length p53as, they teach the art known presence of full length p53as and that it's study was critical to future studies of p53. Han et al. further provide primers unique to p53as and identify the unique regions. Han et al. do not clone full length p53as, however, it is not required of a 103 reference to completely disclose the invention and the failure to do so does not render the obviousness of the invention based on that reference based on hindsight. Given the knowledge of p53as and it's criticality in the studies of p53, plus the primers necessary to isolate the p53as cDNA, plus the art-known procedures for doing so and incorporation into baculovirus for mass production to facilitate study supplied by Lee et al., it would have been *prima facie* obvious to one of ordinary skill in the art to further the cloning of Han et al. to include full-length p53as, with a reasonable expectation of success given the provision of primers for doing so and the art-standard techniques of Lee et al. Further, one would be motivated to do so given the suggestion

by Han et al. that it would be critical to include p53as in the study of p53 and the teachings of Lee et al. directed to obtaining large quantities of protein for study.

NO CLAIM IS ALLOWED.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-2731. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**paula.hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler, Ph.D.
Primary Examiner
January 28, 2000